Chapter 1

Desquamative Gingivitis

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Additional information is available at the end of the chapter

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Abstract

Desquamative gingivitis (DG) is characterized by erythematous, epithelial desquamation, erosion of the gingival epithelium, and blister formation on the gingiva. DG is a clinical feature of a variety of diseases or disorders. Most cases of DG are associated with mucocutaneous diseases, the most common ones being lichen planus, mucous membrane pemphigoid, and pemphigus vulgaris. Proper diagnosis of the underlying cause is important because the prognosis varies, depending on the disease. This chapter presents the underlying etiology that is most commonly associated with DG. The current literature on the diagnostic and management modalities of patients with DG is reviewed.

Keywords: gingival diseases/pemphigus/pemphigoid, benign mucous membrane/lichen planus, oral/hypersensitivity/autoimmune diseases

1. Introduction

Manifestations of desquamative gingivitis (DG) include erythematous gingiva, epithelial desquamation, and erosion of the gingival epithelium, as well as blister formation on the gingiva [1, 2] (**Figure 1**). The DG lesions may be localized or generalized and may extend into the alveolar mucosa. Similar lesions are often found on the buccal mucosa, tongue, and palate in the oral cavity. The signs of DG are clearly different from those of dental plaque-induced gingivitis. Patients having DG may be asymptomatic or symptomatic [3]. Most symptomatic patients complain of mild or moderate oral discomfort, gingival soreness, or a burning sensation [4, 5]. DG occurs more often in females than males; approximately 80% of the patients are female [4–8]. Most patients with DG are middle-aged and older, although rare cases have

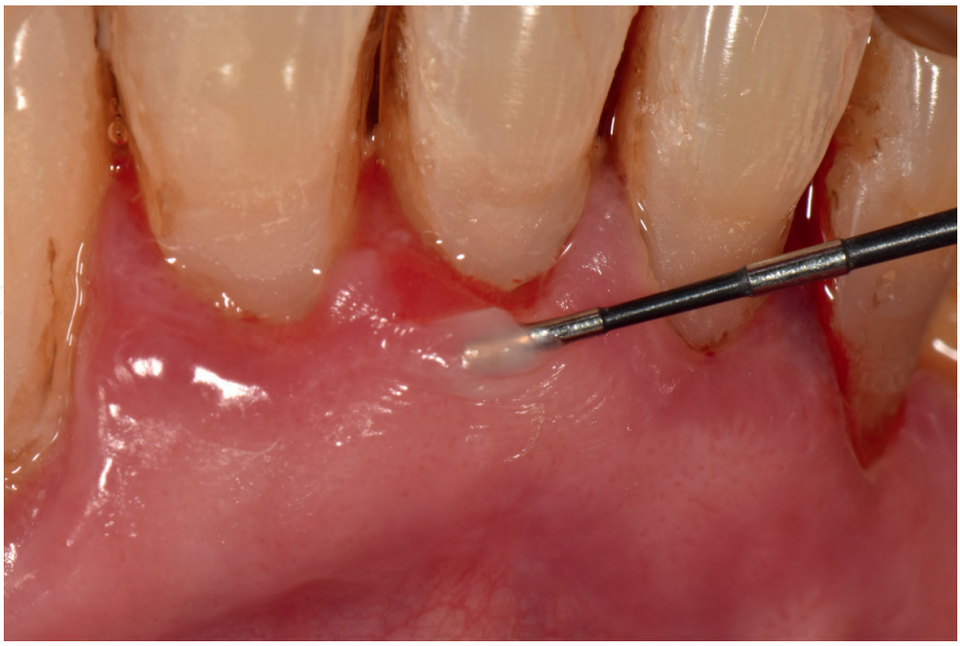

Figure 1. Desquamative lesions on the attached gingiva. Gentle palpation with the periodontal probe elicited some desquamation of the gingival surface (positive Nikolsky's sign).

been observed in children [4, 6, 8, 9]. Early investigators believed that there was a single etiology for DG. However, it is apparent that the condition is a nonspecific manifestation of several diseases or disorders and therefore has multiple etiologies [1, 2]. Most cases of DG are associated with mucocutaneous diseases, the most common ones being lichen planus (LP), mucous membrane pemphigoid (MMP), and pemphigus vulgaris (PV) [1, 2, 4–8, 10, 11]. A variety of other potential causes, such as lupus erythematosus [12], mixed connective tissue disease [5, 10], graft versus host disease [13], erythema multiforme [14], epidermolysis bullosa [15, 16], epidermolysis bullosa acquisita [17], Kindler syndrome [18], chronic ulcerative stomatitis [10, 19, 20], lichen planus pemphigoides [21, 22], plasmacytosis [23], plasma cell gingivitis [24], orofacial granulomatosis [25, 26], foreign body granulomas [27], candidal infection [28], and linear IgA disease [29, 30], may cause DG lesions. Factitious injury of the gingiva may also present with clinical features consistent with DG [31–34], which was suggestive of mucocutaneous diseases including MMP [32, 33] or PV [34]. Contact stomatitis due to dental hygiene products, dental materials, or food flavorings and preservatives may mimic DG [1, 11, 25, 35–39], while several systemic disorders, including Crohn's disease [40], psoriasis [41–43], sarcoidosis [44], and adverse drug reactions [38, 45], may possess some but usually not all of the clinical features of DG.

2. Diagnosis

It is very important to accurately diagnose diseases or disorders causing DG because the prognosis varies widely, depending on the cause. Although PV rarely occurs, it is a potentially life-threatening disease, so it is important to diagnose and treat it in its early stages. Airway obstruction due to laryngeal scarring and blindness due to conjunctival scarring

would certainly deteriorate the quality of life for MMP patients. Early recognition and treatment of the lesions can prevent serious complications. Histopathological examination and direct immunofluorescence (DIF) testing of biopsied tissues are often required to determine the underlying etiology of DG [6–8, 10]. For histopathological study, the biopsy site should be selected from an area of intact epithelium and include perilesional tissue. This may require two separate biopsies, one lesional and one non-lesional. The perilesional tissue or non-lesional biopsy site should show a nonspecific inflammatory response in suspected non-autoimmune disorders such as LP, erythema multiforme, foreign body gingivitis, factitious disorder, and contact stomatitis [1, 7, 10]. In contrast, the DIF test should be performed on normal-appearing tissue rather than perilesional sites in suspected autoimmune diseases such as MMP, PV, and chronic ulcerative stomatitis [1, 7, 10, 46, 47]. Since immune deposits in autoimmune bullous disease are present in all oral tissue, a positive result from DIF tests may be obtained from biopsies taken from distant normal mucosa [46]. The DIF test is considered to be the best diagnostic evidence for MMP, PV, chronic ulcerative stomatitis, and other autoimmune disorders; therefore, DIF testing is often essential in obtaining a final diagnosis since clinical features may be so similar [6–8, 10, 47, 48]. On the other hand, DIF findings are supportive but not diagnostic for LP, psoriasis, lupus erythematosus, and mixed connective tissue disease because the DIF features of these diseases can also be found in other conditions [6, 10, 48]. A negative result from DIF tests should be anticipated in biopsies of contact stomatitis [1].

Biopsy sites appearing to have an intact epithelial surface should be selected. If lesions are present at several mucosal sites, including the gingiva, it is usually best not to use the gingiva for the biopsy [1, 49, 50]. However, in approximately half of DG cases, the gingiva was the only site of involvement [50, 51]. In these cases, the gingiva should be selected for the biopsy. Rees and Burkhart [1] described the six steps to be considered when a gingival biopsy is required in DG patients. They highlight the importance of careful site selection for gingival biopsies in order to obtain diagnostic tissue samples. An inadequate surgical site selection may easily lead to the loss of the gingival epithelium, since the biopsied gingival tissue is thin and tends to be fragile. The stab-and-roll biopsy technique is a procedure specially designed to prevent the epithelium from being removed from the biopsy specimen [1, 46, 52]. This biopsy technique prevents the occurrence of lateral shear forces. The operator applies gentle pressure on the gingiva with the tip of a #15 blade until the bone surface is reached and then the blade is rolled from the tip along the entire cutting edge. If a larger specimen is needed, the tip of the blade can be repositioned and the rolling stroke extended. The gingival epithelium was well maintained, and the relationship with the underlying connective tissue was diagnostic from the gingiva of DG patients using the stab-and-roll biopsy technique [1, 46, 52].

3. Oral mucosal diseases or disorders that are associated with DG

3.1. Lichen planus (LP)

LP is a relatively common, T-cell-mediated chronic inflammatory disease of unknown etiology. LP commonly occurs in middle-aged and older people, and women are affected more frequently

than men [53, 54]. The lesions are found in multiple regions including the skin, genitalia, or oral mucosa, although they are confined to the gingiva alone in some cases [53–56] (**Figures 2** and **3**). In many instances, atrophic, ulcerative, and bullous forms are combined as erosive LP. The reticular, popular, and plaque-like forms of LP are often asymptomatic, whereas erosive forms may be quite painful when a patient is eating spicy foods or performing oral hygiene procedures [53–55, 57] (**Figures 4–6**). For these reasons, erosive LP usually requires treatment. Histopathologically, specimens may demonstrate hyperortho- or hyperparakeratosis, degenerative changes to the basal cells, and band-like subepithelial infiltrate composed of lymphocytes [11] (**Figure 7**). When available, DIF testing is also valuable in establishing the diagnosis, although DIF findings are only suggestive, rather than diagnostic, of LP [6, 10, 48, 58]. Characteristic DIF findings in oral LP include a linear pattern of anti-fibrin or anti-fibrinogen in the basement membrane zone and, to a lesser degree, the presence of IgM or IgG deposits in cytoid bodies [6, 10, 48, 58] (**Figure 8**).

3.2. Mucous membrane pemphigoid (MMP)

MMP is an autoimmune, subepithelial blistering disease that affects mucous membranes. Most patients with MMP are between 60 and 80 years of age [59–61]. However, on relatively rare occasions, MMP has been reported in children [9]. Women are affected nearly two times more frequently than men [59–61]. MMP can involve any oral mucosal site, although the gingiva is affected far more often than other oral tissues [52, 59–62] (**Figures 9–13**). In more than half of early developing cases, the gingiva is the only site of lesions [61, 63]. Extraoral areas including the conjunctiva, skin, pharynx, nose, larynx, genitalia, anus, and esophagus may also be affected [52, 62, 64, 65]. Scarring of the mucous membranes is often considered the clinical hallmark of MMP, although scarring is rarely a feature of oral MMP [52, 64, 65].

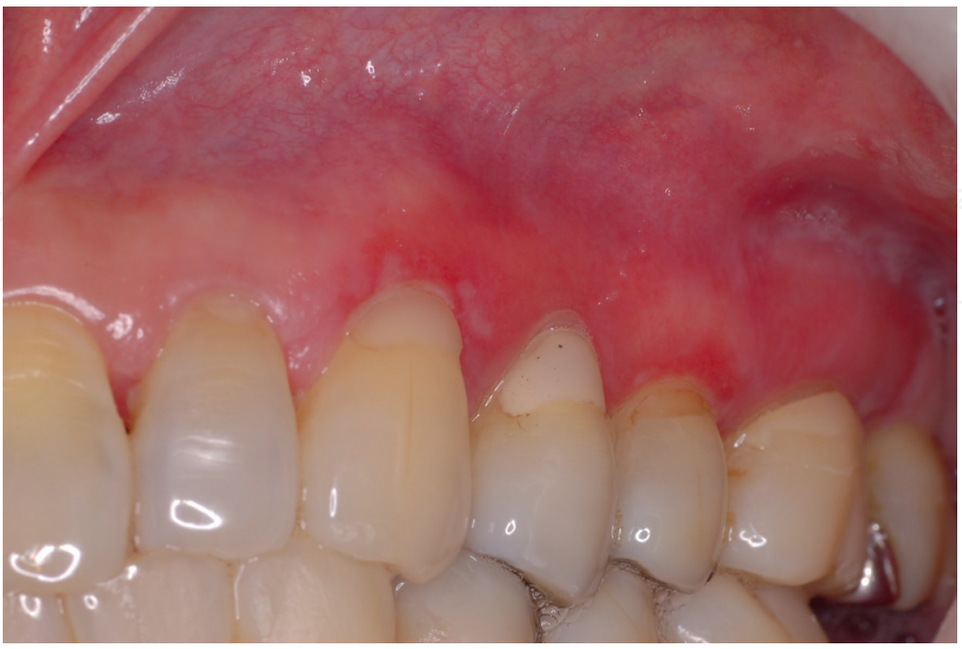

Figure 2. Desquamative gingivitis associated with oral lichen planus. Erythematous lesions on the attached gingiva.

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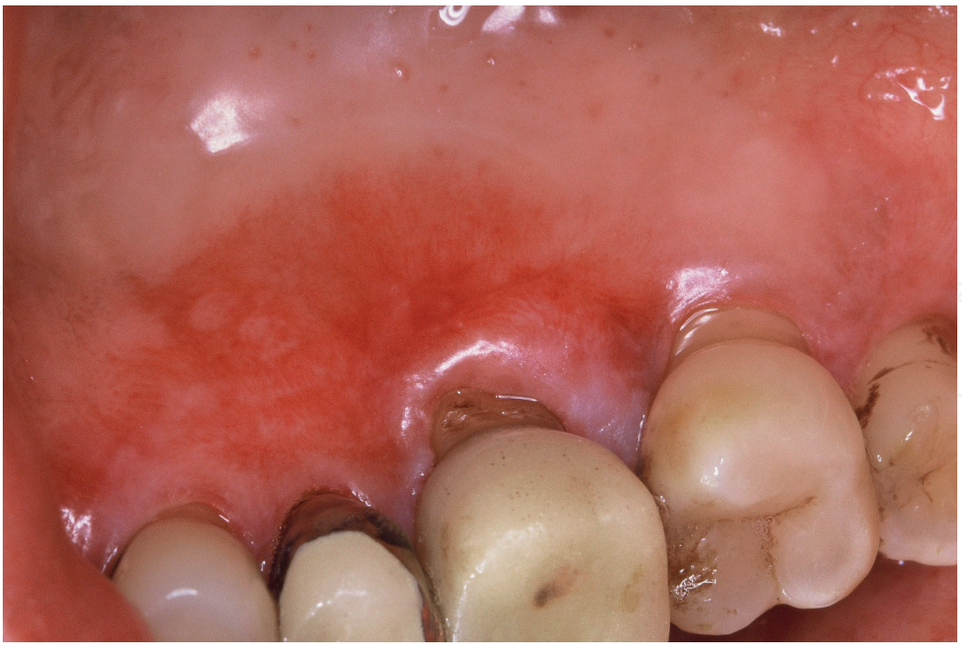

Figure 3. Desquamative gingivitis associated with oral lichen planus. Patchy erythematous lesion was found on the palatal mucosa.

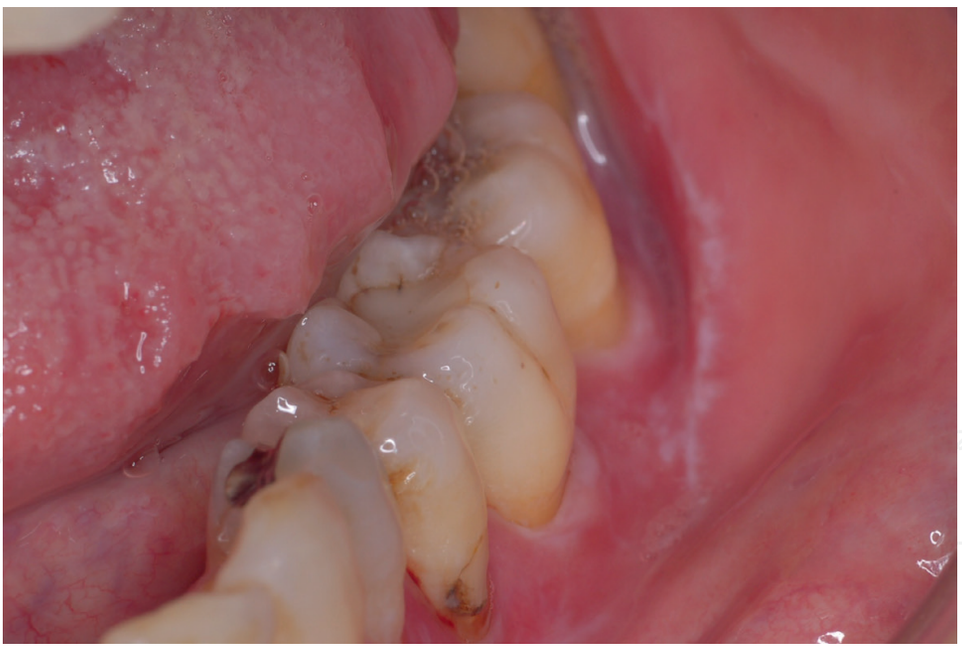

Figure 4. Desquamative gingivitis associated with oral lichen planus. Reticular lesions of buccal mucosa in addition to gingiva.

Multiple target antigens of MMP were identified in cell-to-basement membrane adhesion components by the presence of circulating autoantibodies in the patients' serum. These antigens include bullous pemphigoid antigens (BP180 and BP230), α6 β4 integrin, type VII collagen, and laminin 332 [62, 63, 66, 67]. The loss of cell-to-basement membrane adhesion

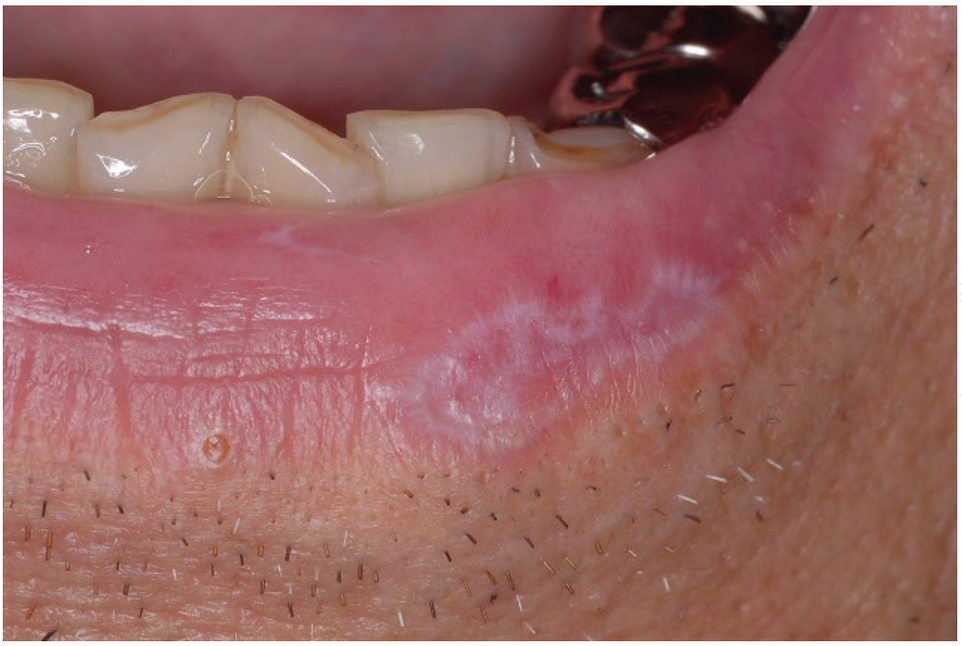

Figure 5. Extraoral lesion associated with oral lichen planus. The reticular lesion was observed on the lip.

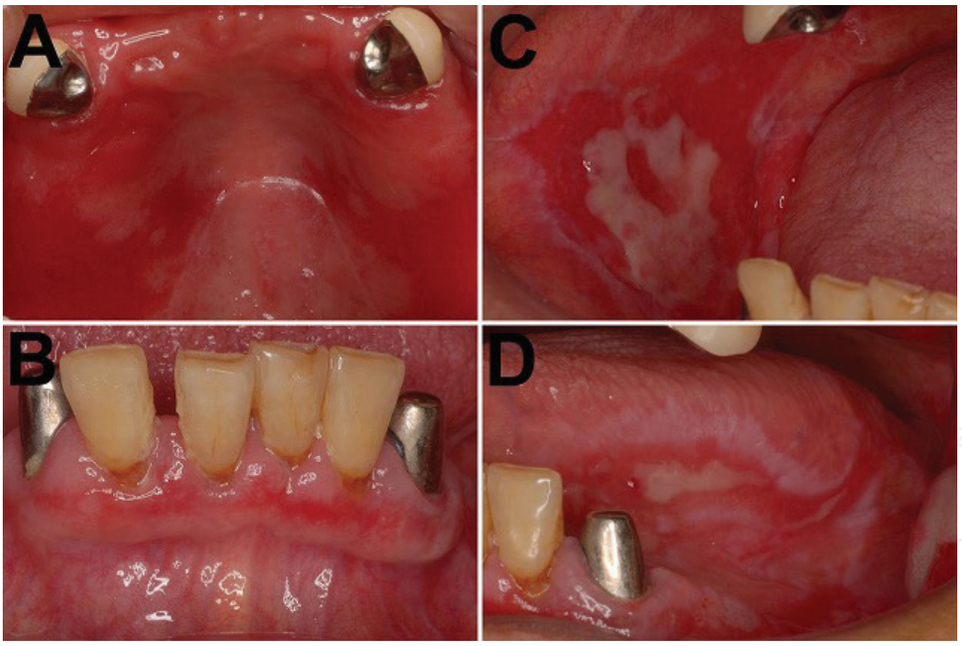

Figure 6. Oral lichen planus patient. The examination revealed diffuse erythematous lesions on the gingiva (A and B). Lesions were also found on the buccal mucosa (C) and tongue (D).

caused by these antibodies may result in subepithelial blistering. Histopathologically, MMP is characterized by subepithelial bulla formation [11] (**Figure 14**). During DIF testing, the linear deposition of complement component C3, IgG, or other immunoglobulin is observed in a linear pattern along the basement membrane zone [48, 62] (**Figure 15**).

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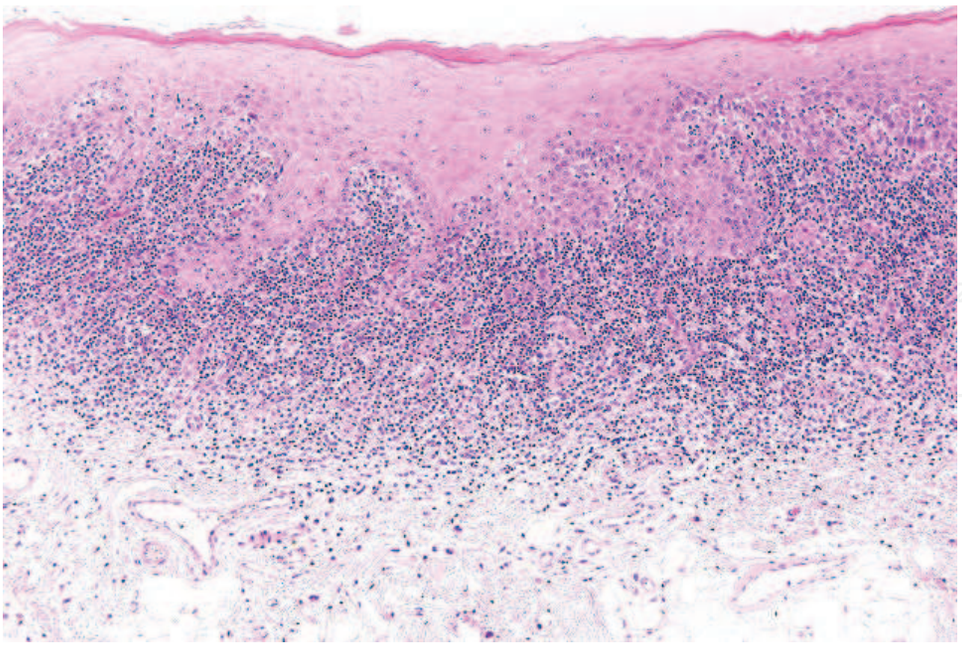

Figure 7. Hematoxylin-eosin-stained section of oral lichen planus. The basal layer liquefaction and shortened rete ridges were found. A band-like infiltration of lymphocytes in the lamina propria was also observed.

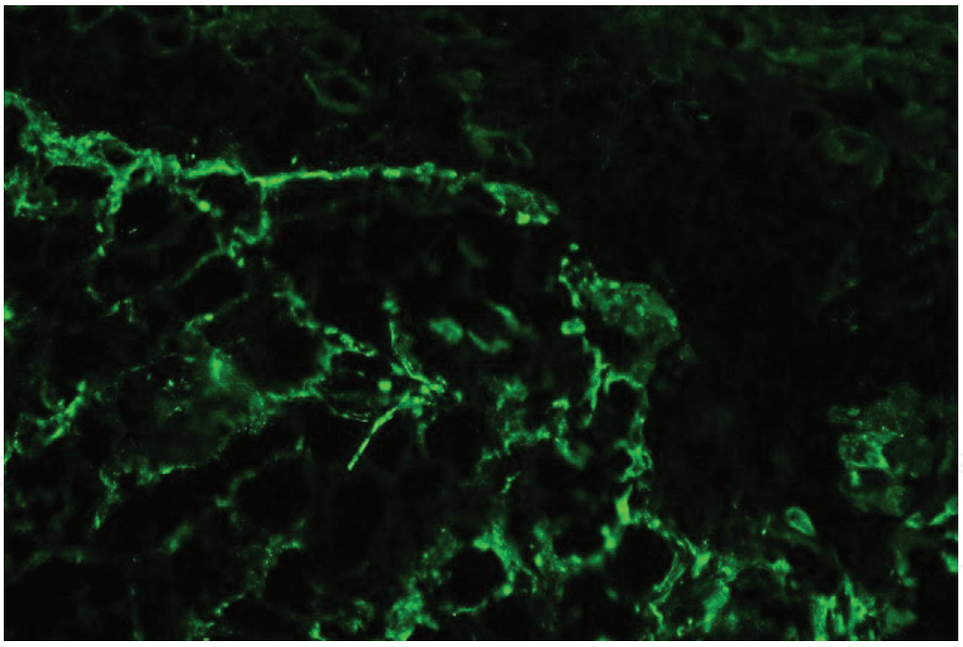

Figure 8. Direct immunofluorescence of oral lichen planus. A linear deposition of fibrinogen at the basement membrane zone was found.

3.3. Pemphigus vulgaris (PV)

PV is an autoimmune blistering disease characterized by acantholysis in the epithelium. Most patients with PV are middle-aged and elderly [68–71]. The disease is equally common in men and women [71], and it is a potentially life-threatening disease [72]. Characteristics

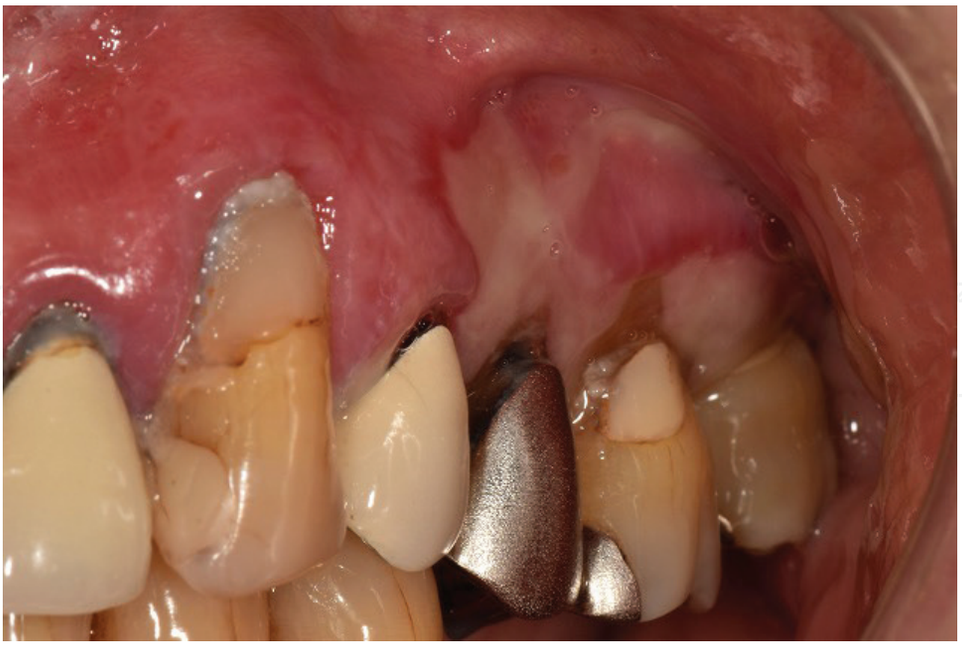

Figure 9. Desquamative gingivitis associated with mucous membrane pemphigoid. Ulcerated gingival surface was observed.

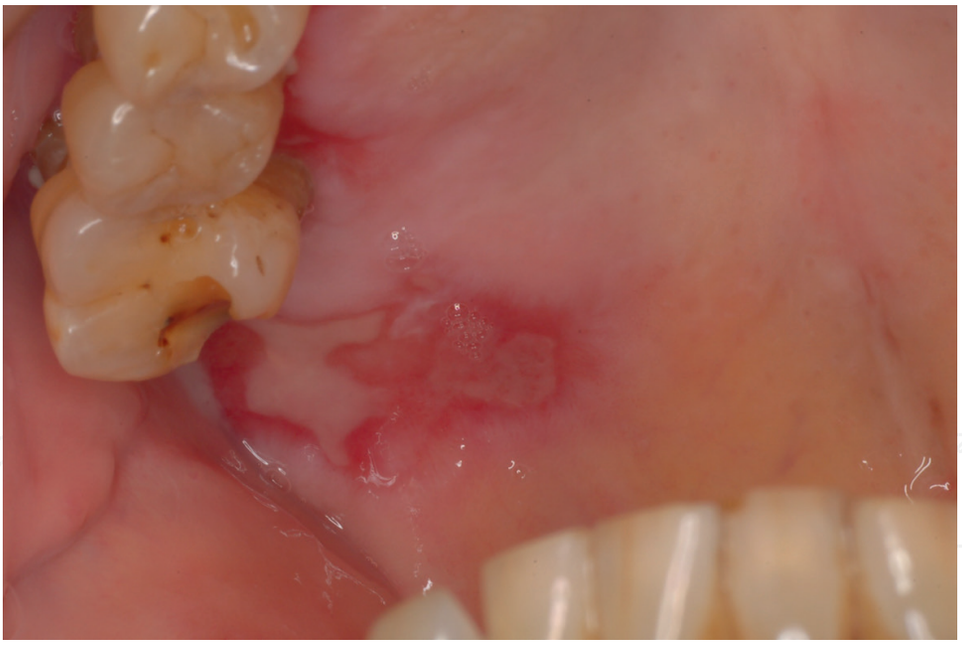

Figure 10. Desquamative gingivitis associated with mucous membrane pemphigoid. Ulceration of the palatal mucosa.

of the PV lesions are flaccid bulla formation, erosion, and ulceration in the skin or mucosa [1, 68] (**Figures 16–19**). PV frequently begins with oral lesions and later progresses to involve the skin [73, 74] (**Figure 20**). Oral lesions are the most common evidence and develop in almost all patients having PV [68, 71]. Lesions may affect the gingiva, and occasionally, the gingiva is the only site of involvement in early lesions [69, 73–75]. Circulating PV autoantibodies

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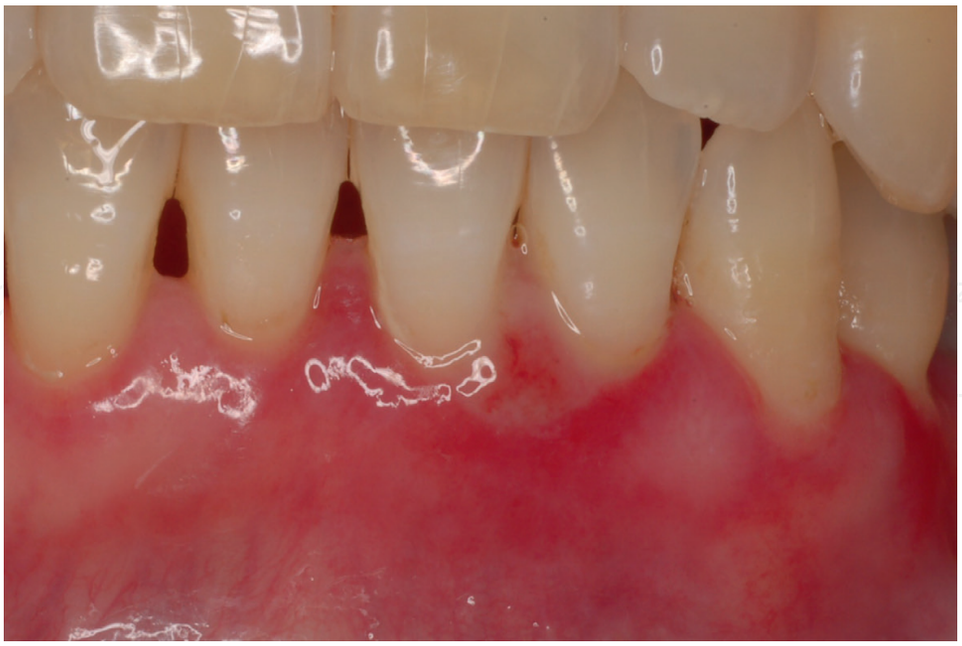

Figure 11. Desquamative lesions featuring gingival erythema associated with mucous membrane pemphigoid.

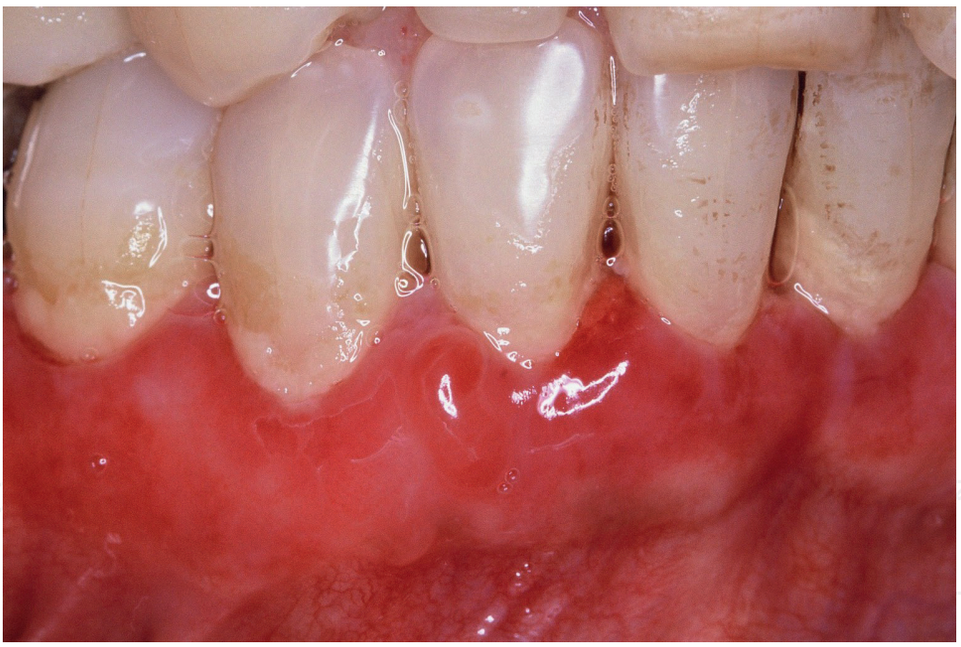

Figure 12. Localized blister formation on the gingiva associated with mucous membrane pemphigoid.

in the serum are pathogenic, and they can cause acantholysis in the epithelium [76]. More than 50 proteins have been reported to specifically react with pemphigus IgG autoantibodies [77], but it has been determined that the principal autoantigens in pemphigus patients are desmogleins, which are the components of desmosomes in the epidermis and mucous membranes [78, 79]. Almost all patients with PV lesions restricted to the oral mucosa have only anti-desmoglein 3 antibody in the serum, whereas patients with advanced cases involving

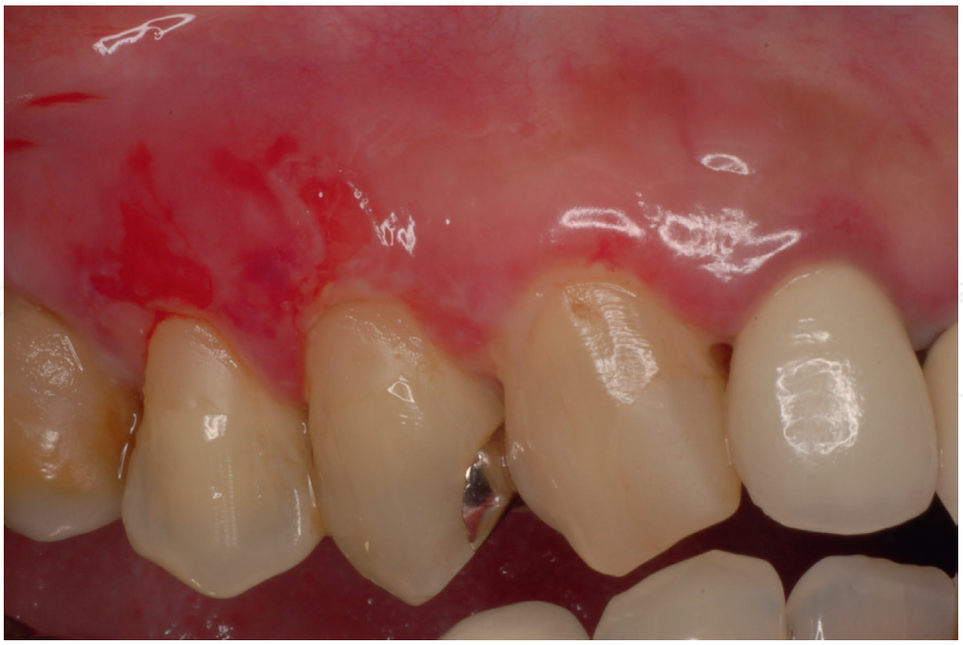

Figure 13. Desquamative lesions on the attached gingiva associated with mucous membrane pemphigoid.

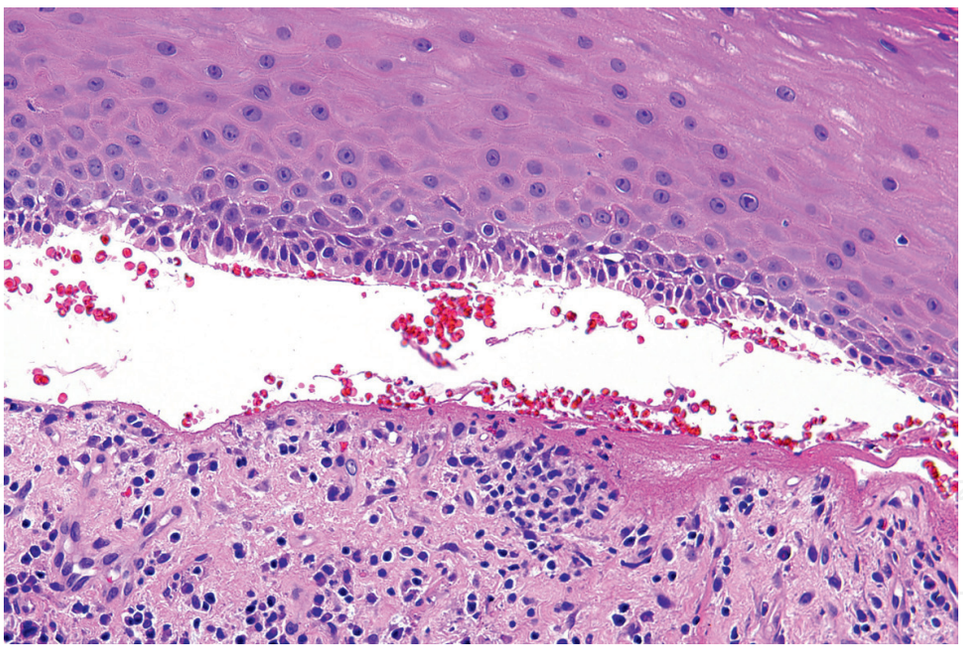

Figure 14. Hematoxylin-eosin-stained section of mucous membrane pemphigoid. A subepithelial blister formation was found.

the oral mucosa and skin may have both anti-desmoglein 3 and anti-desmoglein 1 antibodies [73, 74]. Histopathologically, PV is characterized by acantholysis and a suprabasilar split in the epithelium [11] (**Figure 21**). Tzanck cells are often found in intraepithelial clefts [80]. In the DIF examination of PV patients, the deposition of IgG and/or C3 is found in the intercellular spaces of the epithelium [48] (**Figure 22**).

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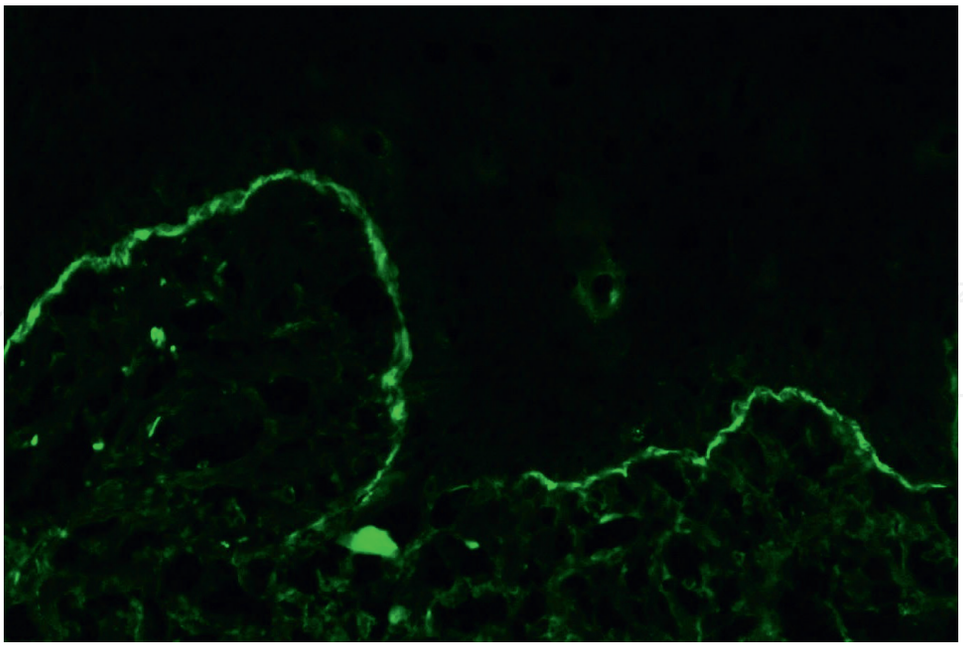

Figure 15. Direct immunofluorescence of the mucous membrane pemphigoid. A linear deposition of IgG at the basement membrane zone was found.

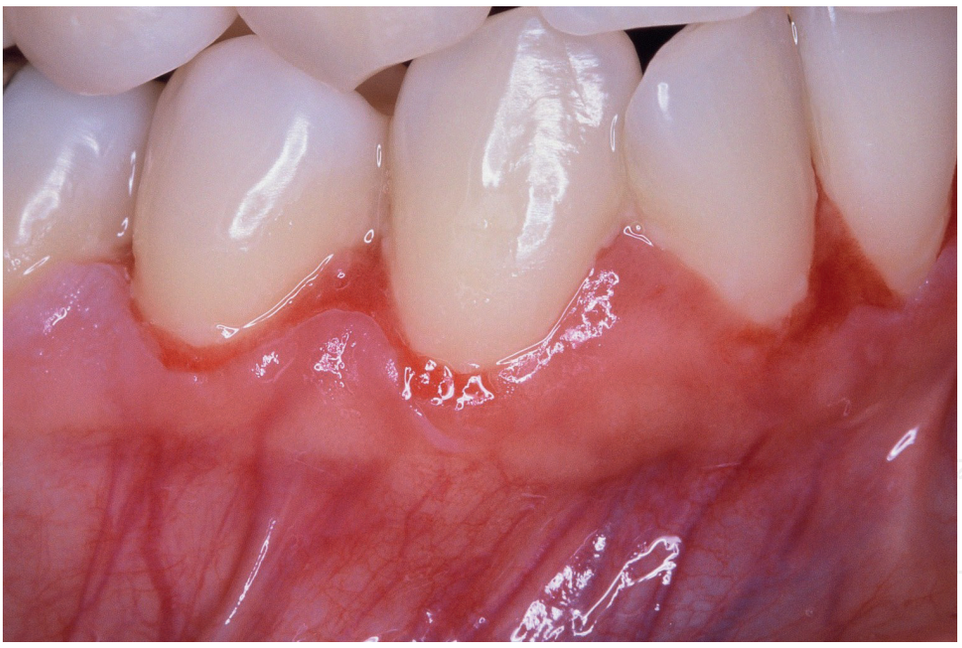

Figure 16. Desquamative gingivitis associated with pemphigus vulgaris. Eroded gingival surface with ragged edges was observed.

3.4. Contact hypersensitivity reactions as cause of DG

Localized or generalized DG is sometimes elicited by contact hypersensitivity reactions to various foodstuffs, preservatives, oral hygiene products, and dental restorative materials [11, 25, 35–39, 81]. Toothpaste hypersensitivity reactions may occur in various oral or perioral

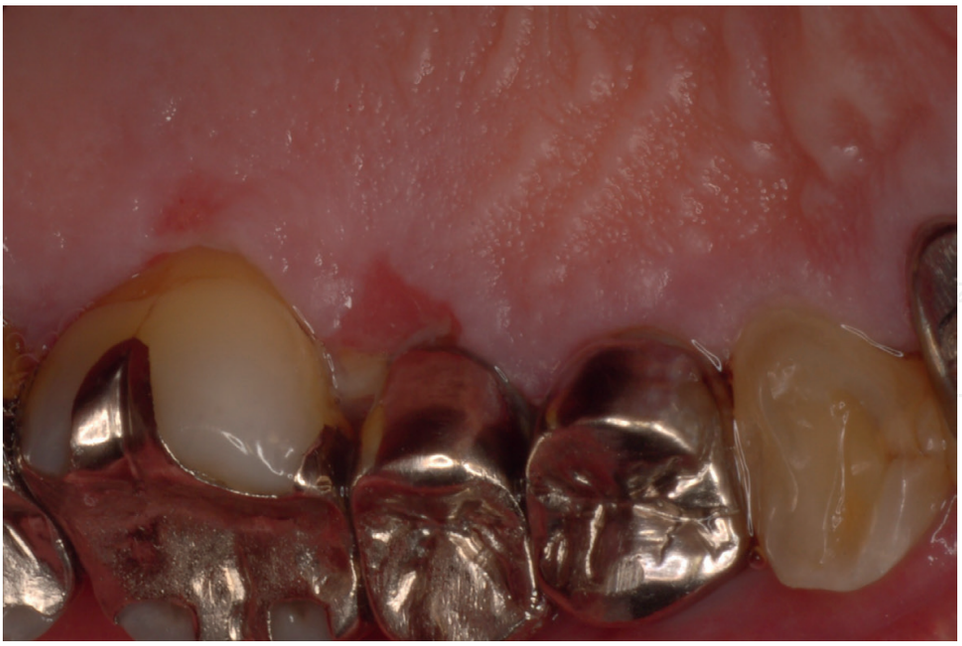

Figure 17. Desquamative gingivitis associated with pemphigus vulgaris. Localized erosions of the palatal mucosa.

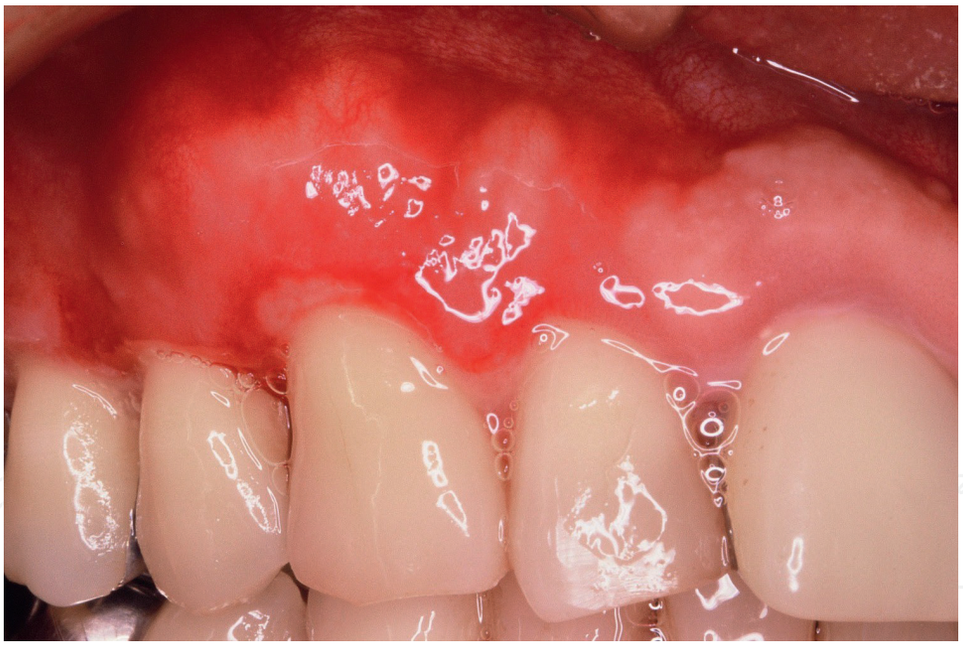

Figure 18. Mild erythema and ulceration of gingiva associated with pemphigus vulgaris.

sites, but the gingiva was the most common site of onset [24, 35, 36, 39, 81] (**Figure 23**). Erythema has been expressed as a "velvet-like appearance of the gingiva" or "fiery red gingiva" [35]. Epithelial sloughing is the most common irritant effect associated with toothpastes and mouthwashes [1, 2, 35, 82] (**Figure 24**). Allergy to dental restorative materials usually causes localized DG in gingival or other mucosal tissues directly contacting the allergen [1, 11]. Gingival contact hypersensitivity lesions are usually not biopsied. However, if a biopsy

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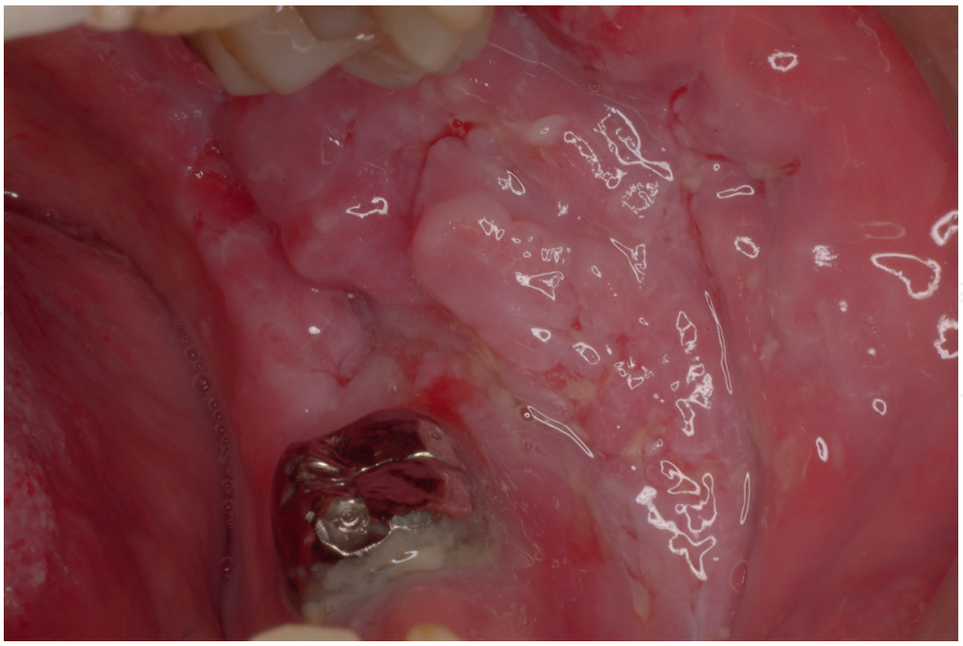

Figure 19. Pseudomembrane-covered erosion of buccal mucosa associated with pemphigus vulgaris.

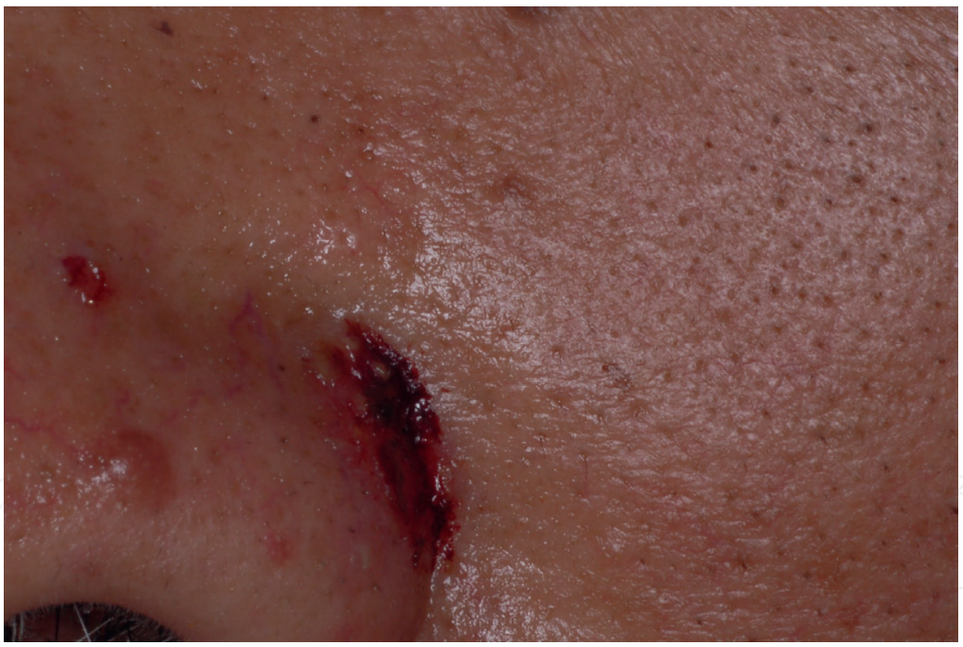

Figure 20. Skin involvement in a desquamative gingivitis associated with pemphigus vulgaris.

is performed, these lesions present with non-specific histopathologic findings with submucosal perivascular inflammatory cell infiltration [11, 35, 36]. The existence of focal granulomatous inflammation and/or multinucleated giant cells in the deep layer of the lamina propria was also described in some cases studying contact hypersensitivity stomatitis [25, 81]. DIF is not indicated because it is routinely negative [11]. To treat contact hypersensitivity reactions, the allergen should be identified and removed. To do so, patients should be questioned

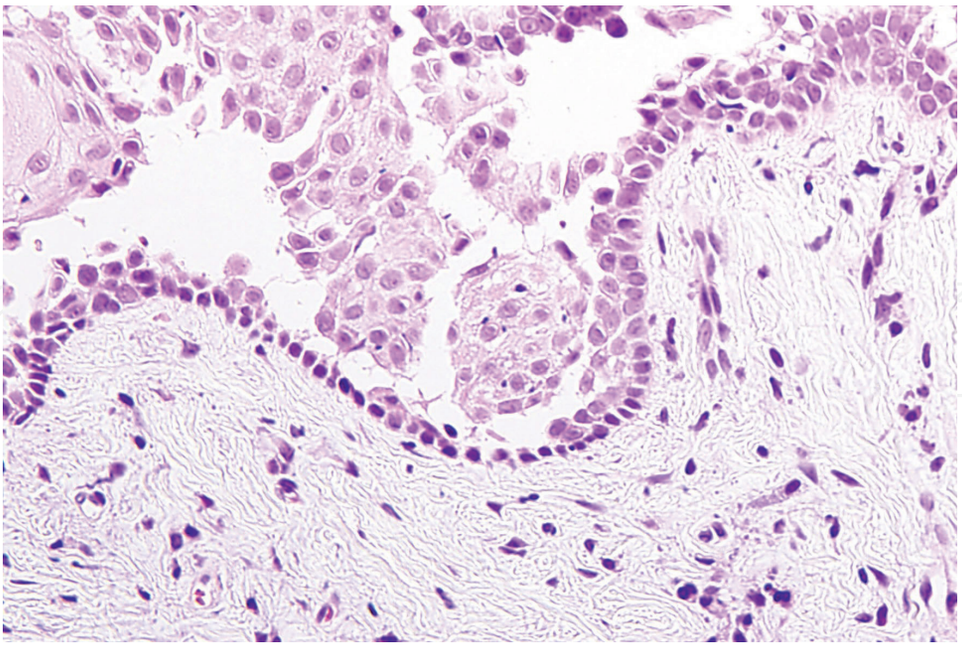

Figure 21. Hematoxylin-eosin-stained section of pemphigus vulgaris. Acantholys was recognized.

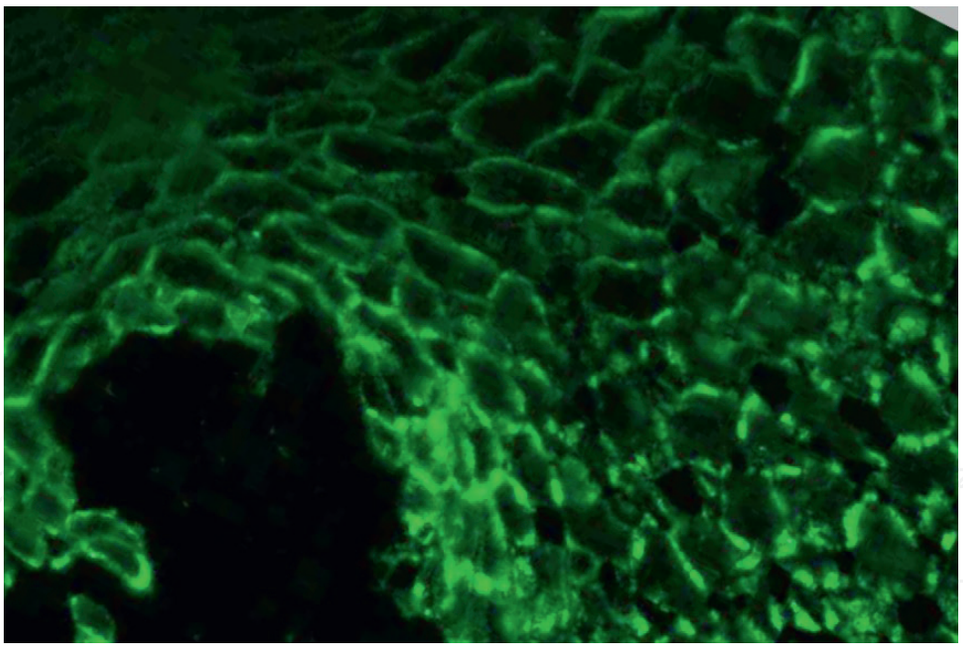

Figure 22. Direct immunofluorescence of pemphigus vulgaris. An intercellular deposition of IgG was seen.

regarding the type(s) of oral hygiene products they use, and a 1–2-week food diary may help identify causative agents [35]. Patch testing may be required to identify the allergen or to confirm a specific allergen in a dental hygiene product or in a dental restoration. Patients are considered to have allergic reactions to a relevant allergen if their patch test results are

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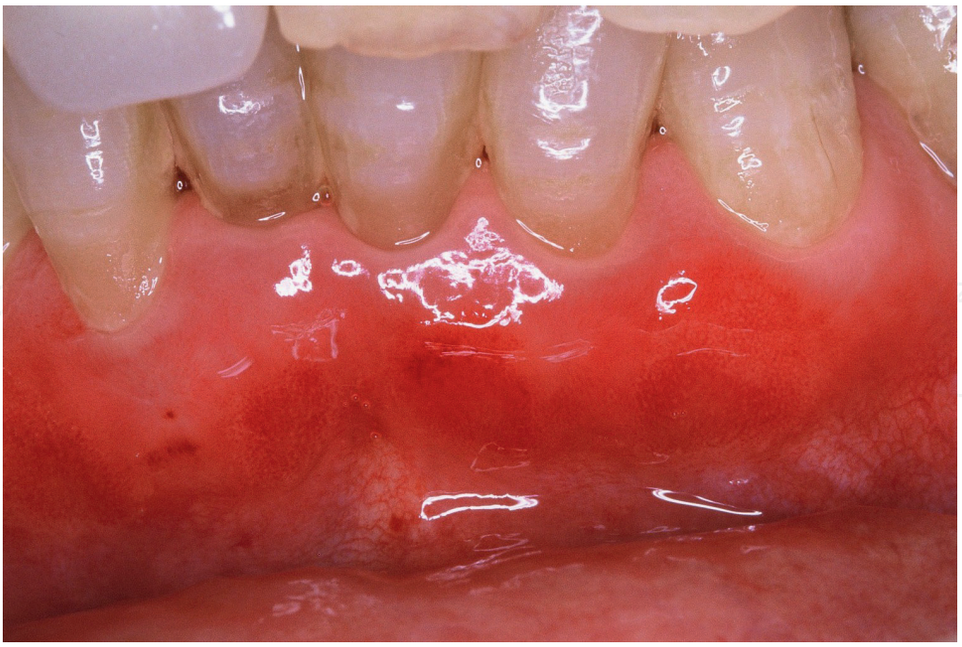

Figure 23. Contact hypersensitivity reactions caused by toothpaste. Localized erythematous and edematous lesions were found on the gingiva.

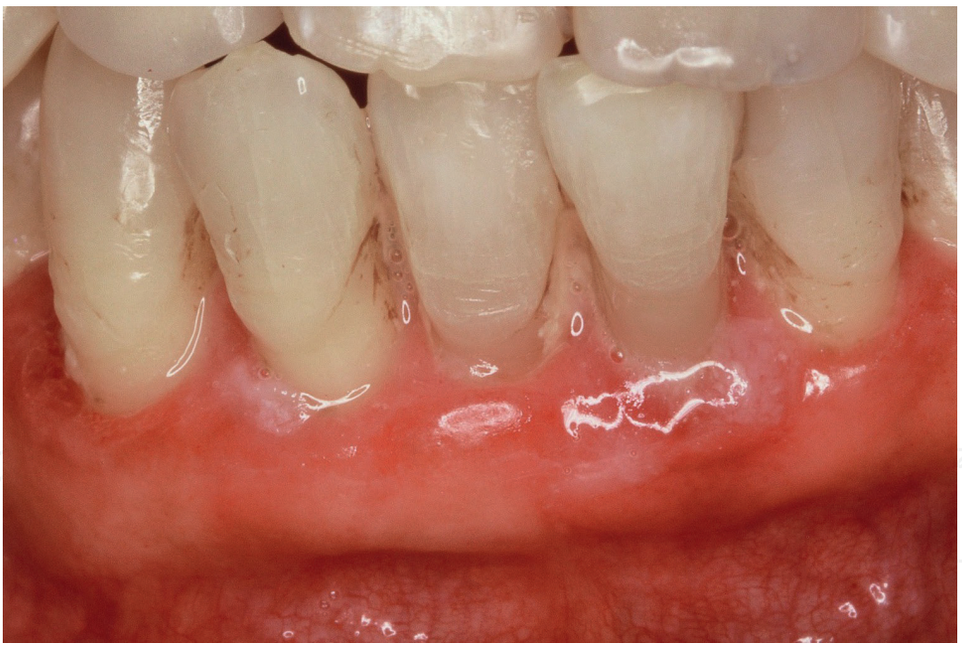

Figure 24. Contact hypersensitivity reactions caused by mouth rinse. Epithelial sloughing was noted.

positive [35, 81]. However, diagnosis of contact hypersensitivity reactions may be confirmed simply by the discontinuation of the causative agent(s) resulting in the remission of clinical signs and symptoms [35, 36, 81].

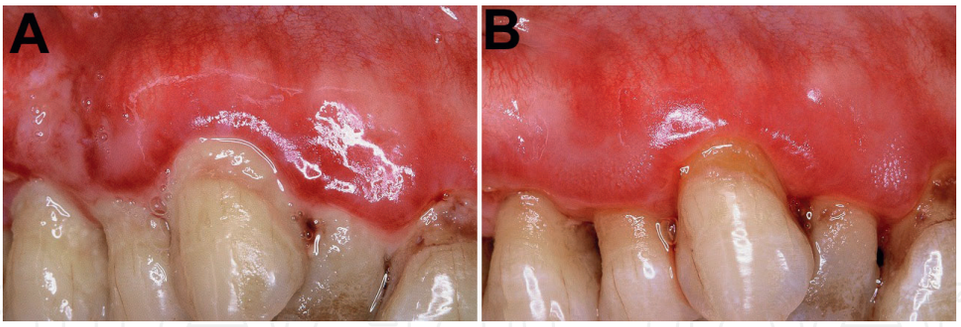

Figure 25. Desquamative gingivitis associated with mucous membrane pemphigoid. The initial examination revealed moderate erythema and swelling of the gingiva with plaque and calculus deposits (A). Treatment response. The condition of the gingiva improved due to a topical corticosteroid therapy combined with effective plaque control (B).

4. Managing DG patients

The specific disease or disorder causing DG, the severity of the gingival lesions, the presence or absence of extraoral involvements, and the medical history of the patient are the key factors in determining the selection of a topical or systemic immunosuppressive therapy [1, 2, 69, 83]. The patients diagnosed as having an autoimmune disease should be closely followed because they may require immediate referral to other health care experts especially if they develop extraoral lesions. After MMP is diagnosed from DG or concomitant lesions, patients should undergo examination by medical specialists including an ophthalmologist and an otolaryngologist, and the presence or absence of extraoral lesions should be determined. PV patients with exclusively oral lesions should be followed closely and referred to other experts immediately if they develop lesions elsewhere on the body. Management of the specific disease or disorder causing DG may best be provided by a specialist in oral medicine, oral pathology, periodontics, or oral surgery, but the dentist may still be responsible for maintaining the dental and periodontal health of the patient. This is important because periodontal and dental considerations are often observed in DG patients, but the literature contains minimal information regarding the periodontal and dental management of these individuals. Plaque-induced gingivitis is almost universal in patients with symptomatic DG, and an effective therapeutic protocol should include non-surgical periodontal therapy consisting of oral hygiene instruction, scaling, and root planting [2, 84–89] (**Figure 25**). We believe that excessively vigorous scaling and root planting can be unnecessarily damaging to DG-affected lesions, and we prefer a sequential gingival management approach that features gentle supragingival and slight subgingival debridement which can be repeated at two-week intervals resulting in gradual improvement in periodontal status until an acceptable level of periodontal health has been achieved. The relationship between the existence of DG lesions and the progression of periodontal diseases is inconclusive, although some but not all studies

demonstrated a correlation between compromised periodontal status and autoimmune bullous diseases affecting the mouth [90–96]. There are several reports on periodontal surgery or dental implant therapy performed on patients having DG [15–17, 73, 97–100]. Tissue sloughing and a lack of tissue elasticity caused by active autoimmune bullous disease can disturb the manipulation of the mucosal flap. Strict mucosal disease control prior to surgery may reduce the surgical complications [101]. Implant therapy is likely to enhance the quality of life in patients with systemic diseases and may help them maintain long-term masticatory function. Patients with DG are often unable to wear tissue-borne prostheses because of discomfort. This tissue irritation and oral pain can be increased if the appliances are ill fitting or damaged. A dental implant-supported prosthesis improves the stabilization of the prosthesis, resulting in a higher degree of comfort. Published case reports indicated that DG patients can be successfully managed with dental implants. These reports suggest that the degree of disease control may be more important than the nature of the disease itself in regard to the effects on osseointegration. Penarrocha et al. [98] reported that implants can be successfully placed and used to support dental prostheses in patients with recessive dystrophic epidermolysis bullosa. A total of 38 implants were placed in six totally edentulous patients. Only one implant failed to achieve osseointegration. The average follow-up from implant placement was 5.5 years. The implant-supported prostheses were associated with improvements in the patients' comfort and function, esthetics and appearance, taste, speech, and self-esteem. Altin et al. [99] presented a case of PV rehabilitation using a successful implant-supported prosthesis with a 32-month follow-up. They concluded that the implant treatment may be considered as a good alternative to a tissue-borne prosthesis in PV patients. Esposito et al. [100] reported implant retained overdentures for two patients with severe oral LP. The patients were often unable to wear tissue-borne prostheses because of the discomfort. There was good integration of the implants with no clinical or radiographic evidence of bone loss, and the soft-tissue/implant response was excellent. Lesions occasionally flared-up but were successfully treated with topical steroids. There was no evidence of potential implant failure as a result of these flare-ups. Although these descriptions of successful management using dental implants for patients with DG are promising, further studies are needed since these were individual case reports.

5. Conclusion

DG is a clinical manifestation that is common to several diseases or disorders. It is important to diagnose the diseases causing DG because the prognosis varies, depending on the disease. Histopathological examination and DIF testing are often required to establish the final diagnosis. The patients diagnosed with autoimmune diseases such as MMP or PV should be closely followed because they must be immediately referred to other experts when they develop lesions on parts of their body other than the oral cavity.

Abbreviations

DG	Desquamative gingivitis
LP	Lichen planus
MMP	Mucous membrane pemphigoid
PV	Pemphigus vulgaris
DIF	Direct immunofluorescence

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